

Guidelines for Reviewers

Small Business Innovation Research (SBIR) Small Business Technology Transfer Research (STTR)

The Center for Scientific Review
National Institutes of Health

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Important Features:

- ❖ Instructions and forms for SBIR and STTR applications appear in the Application for a Public Health Service Grant¹ (PHS 398; revised 05/2001), and abbreviated instructions are in the Omnibus Solicitation of the National Institutes of Health, Centers for Disease Control and Prevention, and Food and Drug Administration for Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Grant Applications² (PHS 2002-2).
- ❖ The NIH has changed the PHS policy to permit institutions with Animal Welfare Assurance to submit verification of Institutional Animal Care and Use Committee (IACUC) approval for competing applications subsequent to peer review, but prior to award.
- ❖ The evaluation of the application's plan for the protection of human subjects from research risks and the plans for the enrollment of women, minorities, and children in the proposed research is now a critical portion of your review.
- ❖ All revised applications (A1 or A2) must include an introduction; one (1) page maximum for Phase I applications, three (3) pages maximum for Phase II applications.

¹ Reviewers should also refer to the Instructions and Application Forms for a Public Health Service Grant (PHS 398; <http://grants.nih.gov/grants/funding/phs398/phs398.pdf> or <http://grants.nih.gov/grants/funding/phs398/phs398.html>) for additional information.

² Reviewers may also refer to the Omnibus Solicitation of the National Institutes of Health, Centers for Disease Control and Prevention, and Food and Drug Administration for Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Grant Applications (PHS 2002-2) (<http://grants.nih.gov/grants/funding/sbirsttr1/index.pdf>) for additional information.

I. General Program Description

The objectives of the SBIR/STTR programs include stimulating technological innovation in the private sector, strengthening the role of small business in meeting Federal Research/Research & Development needs, increasing private sector commercialization of innovations developed through Federal SBIR/STTR R&D, increasing small business participation in Federal R/R&D, and fostering and encouraging participation by socially and economically disadvantaged small business concerns and women-owned business concerns in the SBIR/STTR programs. The unique feature of the STTR program is the requirement for the small business concern applicant organization to formally collaborate with a research institution in Phase I and Phase II.

The SBIR and STTR programs differ in significant ways. First, the STTR program requires the small business: (1) to have a formal collaboration with researchers at a university or other non-profit research institution, and (2) to play a significant intellectual role in the conduct of the STTR project. Second, only the SBIR program stipulates that the Principal Investigator must have their primary employment with the small business. Therefore, the Principal Investigator on an STTR may be from the small business or the research institution *as long as they have a formal appointment with or commitment to the applicant small business, which is characterized by an official relationship between the small business and the Principal Investigator.*

A. SBIR/STTR Programs: First Two Phases

Phase I: Feasibility (type 1R41 and type 1R43 applications)

The objective of Phase I is to establish the technical/scientific merit and feasibility of the proposed R/R&D efforts and to determine the quality of performance of the small business grantee organization prior to providing further Federal support in Phase II.

- ❖ Preliminary data are not required.
- ❖ SBIR Phase I awards normally may not exceed \$100,000 total costs³ for a period normally not to exceed 6 months. The total amount of all contractual costs and consultant fees normally may not exceed 33% of the total costs requested.
- ❖ STTR Phase I awards normally may not exceed \$100,000 total costs³ for a period of 1 year.
- ❖ These award levels for duration and total costs are statutory guidelines, not ceilings. Deviations from the guidelines are acceptable, but must be justified in the application.
- ❖ For STTR awards, at least 40% of the work must be performed by the small business and 30% of the work must be performed by the research institution.
- ❖ For STTR awards, the principal investigator must spend a minimum of ten percent effort on the grant.

Phase II: Full Research/R&D Effort (type 2R42 and type 2R44 applications)

The objective of the Phase II is to continue the research or R&D efforts initiated in Phase I. Evaluation is based on the results of Phase I, scientific and technical merit, and commercial potential and societal impact of the Phase II application. Reviewers may access additional information on Phase II applications.⁴

- ❖ SBIR Phase II awards normally may not exceed \$750,000 in total costs³ for a period normally not to exceed 2 years. The sum of the consultant costs and contractual costs normally may not exceed 50% of the total costs requested.
- ❖ STTR Phase II awards normally may not exceed \$500,000 total costs³ for a period normally not to exceed 2 years.

³ Total costs are the sum of direct costs, facilities and administration costs, and a negotiated fixed fee.

⁴ Reviewers should refer to the SBIR Phase II Grant Application Major Policy Changes and Program Reminders (<http://grants.nih.gov/grants/funding/sbir2/polchng.htm>), the SBIR Phase II Grant Application Introduction and Instructions (<http://grants.nih.gov/grants/funding/sbir2/index.htm>), and the STTR Phase II Grant Application Instructions (<http://grants.nih.gov/grants/funding/sttr2/index.html>) for additional information.

- ❖ These award levels for duration and total costs are statutory guidelines, not ceilings. Deviations from the guidelines are acceptable, but must be justified in the application.
- ❖ For an STTR award, at least 40% of the work must be performed by the small business and 30% of the work must be performed by the research institution.
- ❖ For STTR awards, the principal investigator must spend a minimum of ten percent effort on the grant.
- ❖ All Phase II SBIR/STTR applications must include a succinct Product Development Plan (Section I.C., below) within the application.⁵

B. Fast-Track Applications (type 1R42 and type 1R44 applications)

The NIH Fast-Track mechanism expedites the award of SBIR and STTR Phase II funding for scientifically meritorious applications that have a high potential for commercialization.⁶ Fast Track incorporates a parallel review option, in which the Phase I and Phase II grant applications are submitted and reviewed together. Preliminary data are not required, but the Phase I of a Fast Track must specify clear, measurable milestones that should be achieved prior to initiating Phase II work.

C. Product Development Plans All Phase II and Fast-Track applications must include a succinct Product Development Plan within the Phase II application.⁵ Product Development Plans (limited to ten pages) should address:

- ❖ Company information: including size; specialization area(s); products with significant sales; and history of previous federal and non-federal funding, regulatory experience, and subsequent commercialization.⁶
- ❖ Value of the SBIR/STTR project, including lay description of key technology objectives, current competition, and advantages compared to competing products or services.
- ❖ Commercialization plans, milestones, target dates, analyses of market size and estimated market share after first year sales and after five years.
- ❖ Patent status or other protections of project intellectual property.

D. Budgets

For Phase I applications which request up to and including \$100,000 in total costs, i.e., the sum of the direct costs, the indirect costs, and the negotiated Fixed Fee, the applicants may submit a non-modular, detailed budget or use features of the Modular Grant Application and Award procedures.

Non-modular budget format

Detailed budgets may be submitted for applications totaling less than \$100,000 and must be submitted for applications totaling greater than \$100,000. SBIR Phase I and Phase II applications must include Form Page 4 and Form Page 5. Costs should be justified on Form Page 5. STTR Phase I and Phase II applications must include Form Page 4, Form Page 5, and the "STTR Research Institution Budget Form Page." This latter page should include the signature of the duly authorized representative of the research institution affirming certifications made by the research institution upon signing the budget page. The total cost of the portion of the project to be performed by the Research Institution should be indicated on Form Page 4 as "Consortium/Contractual Costs." You should determine whether the percent effort listed for the Principal Investigator is appropriate for the work proposed. Is each budget category realistic and justified in terms of the aims and methods? Information for other items in a Phase I or Phase II application⁷ may be requested by the awarding component if the likelihood exists for the application to be funded.

⁵ SBIR/STTR applications are submitted on the PHS 398 forms; the Product Development Plan should be included as Section J and is excluded from the 25 page limit.

⁶ Commercialization is defined in PHS 398 and PHS 2002-2 as "[t]he process of developing markets and producing and delivering products for sale (whether by the originating party or by others); as used here, commercialization includes both government and private sector markets."

⁷ Information on institutional base salary for personnel, salaries requested, fringe benefits, total personnel costs requested, and Other Support is NOT required at the time an SBIR/STTR application is submitted.

Modular budgets (requests up to \$100,000 total costs³)

The NIH is employing features of the Modular Grant Application and Award procedures under its SBIR/STTR programs for SBIR/STTR applications requesting up to \$100,000 in total costs.³ For modular SBIR applications, only the "Modular Budget Format Page" is required.⁸ For modular STTR applications, the "Modular Budget Format Page" plus the "Research Institution Certification Format Page" are required. The latter page should note the Direct and the Facilities and Administrative Costs; these total costs should be included in the total costs on the "Modular Budget Page." Reviewers should evaluate these modular budgets on the basis of a general, expert estimate of the total costs and resources required to carry out the proposed research in the requested period, rather than on the basis of detailed categorical costs. You should determine whether the percent effort listed for the Principal Investigator is appropriate for the work proposed. Review panel recommendations for SBIR/STTR modular budgets need not conform to modules of \$25,000.

Multi-year Phase I budgets

Multi-year Phase I budget requests that exceed the normal guidelines in terms of amount and duration are allowable for certain SBIR/STTR projects,⁹ if the requests are well justified or stipulated in a specific Program Announcement.

E. Just-in-Time Considerations

Certain items required for a grant application are termed "Just-in-time." These items are not required prior to the review of the application, but will be routinely requested by the awarding component prior to making the grant award.

- ❖ Human Subjects Assurance (item 4b.) and Institutional Review Board (IRB) approval.
- ❖ Institutional Animal Care and Use Committee (IACUC) approval (item 5a.) date.
- ❖ Documentation to establish the "primary employment" of the Principal Investigator with the applicant small business concern (SBIR only).
- ❖ Documentation regarding the performance site(s) of the applicant small business concern as shown on the Face Page of the application, if that site(s) is not owned by the applicant organization.
- ❖ "Other support" for the Principal Investigator and the other "Key Personnel Engaged on the Project" named on Form Page 2, excluding consultants.

II. Review Procedures

Grant applications submitted to NIH are subjected to a peer review process involving two sequential steps that are required by law. The first step is performed by the Scientific Review Groups (SRGs), composed primarily of non-federal scientists, physicians, and engineers (from academia and industry) who are selected for their expertise and stature in particular scientific fields. The Scientific Review Administrator (SRA) is the designated government official responsible for ensuring that each application receives a fair review, according to NIH policy. The second step is performed by the National Advisory Council or Board of the potential awarding component to which the grant application is assigned.

The first task of the SRGs is to make a recommendation for each application on the basis of the SRG's evaluation of the application's scientific and technical merit, potential for commercialization and/or

⁸ For modular SBIR budgets submitted on the PHS 398 forms, the "Modular Budget Format Page" is required, but the "Detailed Budget for Initial Budget Period" (Form Page 4) and the "Budget for Entire Proposed Project Period" (Form Page 5) are NOT required. For modular STTR budgets submitted on PHS 398 forms, the "Modular Budget Format Page" and the "STTR Research Institution Certification Format Page" are required, but the "STTR Research Institution Budget Form Page" and the "Budget for Entire Proposed Project Period" (Form Page 5) are NOT required.

⁹ Instructions to applicants submitting multi-year Phase I budgets on PHS 398 forms are available on the Internet at <http://grants.nih.gov/grants/funding/phs398/phs398.pdf>.

societal benefit.¹⁰ The second task of the SRGs is to make budget recommendations concerning time and dollar amounts that are appropriate for the work proposed.¹⁰

A. Streamlining

NIH uses a numerical scoring range from 100 (most meritorious) to 500, and a streamlining procedure¹¹ to determine those applications that the SRG considers to be in the "upper" and "lower" halves. Applications in the "upper half" are discussed by the SRG and *generally* receive a score between 100 and 300; applications that generally would have received a score between 300 and 500 are not discussed and receive an "unscored" designation. At *any* time during the meeting, *any* SRG member may identify an application that they believe should be discussed and scored.

In accordance with federal regulations, the Principal Investigator clearly must be responsible for the scientific and technical direction of the project. When the Principal Investigator does not have sufficient qualifications to assume this role, the application should be streamlined.

B. Scoring

For applications that are not streamlined, each member records on a scoring sheet a numerical rating that reflects his/her opinion of the merit of each application. Numerical scores are assigned by reviewers in increments of 0.1. In special circumstances, a member may record a non-numerical rating such as NP (Not Present), AB (Abstention), or CF (Conflict of Interest), as appropriate.

Deferral

An application should be deferred if insufficient information exists to make a recommendation. This includes missing sections on human subjects and vertebrate animals. The applicant may be requested to submit additional information, or in special cases a project site visit (applicable to Phase II applications only) may be recommended.

Not Recommending for Further Consideration¹²

The SRG may recommend an application for "no further consideration" in rare cases where 1) the application lacks significant and substantial merit, or 2) the research risks are sufficiently serious and protections against the risks are so inadequate as to consider the proposed research unacceptable on ethical grounds. The decision for "NRFC" must be made by majority vote of the SRG.

C. Fast Track Applications

In most cases, a single score should be assigned to a Fast Track application to reflect the reviewers' enthusiasm for the entire project. The SRG should 1) evaluate the goals that will be achieved during Phase I and the ability of the applicant to demonstrate their probable achievement in a convincing way, and 2) discuss their appropriateness for determining the feasibility of the Phase I. The SRG also may recommend additional milestones that should be achieved before progressing to the Phase II project. In some cases, the SRG may review and score only the Phase I portion of a Fast Track application, if:

- ❖ the application does not include a Product Development Plan that includes the four items listed in Section I.C;
- ❖ the application does not contain clear, measurable Phase I goals that are appropriate for demonstrating feasibility; or
- ❖ the Phase II project is significantly less meritorious than the Phase I project.

¹⁰ Reviewers may refer to the document "Review Procedures for Scientific Group Meetings" for additional information at <http://www.csr.nih.gov/guidelines/proc.htm>.

¹¹ The streamlining procedure for NIH is described in the document entitled "Streamlined Review Procedures Used in CSR" at <http://www.csr.nih.gov/REVIEW/streamln.htm>.

¹² Reviewers should refer to the OER Policy Statement 1996-04, "Fundability of Grant Applications Designated as Unscored or Not Recommended for Further Consideration" at http://odoerdb2.od.nih.gov/oer/policies/oer_announce_1996_04.htm for additional information.

If the SRG scores only the Phase I, then only material from the Phase I application may be used in determining the priority score.

III. Conflict of Interest

A conflict of interest in scientific peer review exists when a reviewer has an interest in an application that may bias or give the appearance of biasing his/her review of it on grounds other than those specified in the review criteria. All reviewers must read the "NIH Conflict of Interest, Confidentiality, and Non-Disclosure Rules and Information for Reviewers of Grant Applications and R&D Contract Proposals" and submit a completed, signed "NIH Pre-Review Certification Form Regarding Conflict of Interest, Confidentiality, and Non-Disclosure for Reviewers of Grant Applications and R&D Contract Proposals" before participating in peer review. A reviewer who has a conflict of interest with an application may not participate in its review, and the appearance of a conflict of interest should be avoided whenever possible.

An SRG must not review an application if:

- ❖ One of its members, or a member's close relative,¹³ is the Principal Investigator or is listed on the budget page in any capacity;
- ❖ One of its members is an owner, officer, or employee in the small business submitting the application; or
- ❖ A member's close professional associate¹⁴ is the Principal Investigator or is responsible for conducting a significant portion of, or has significant intellectual input into, the planned research.

An SRG member must leave the room during the discussion of an application:

- ❖ Submitted by a small business from whom the member has received or could receive direct financial benefit—of any amount—that is related to the project under review, but is not derived from employment;
- ❖ Submitted by a small business from whom the member has received or could receive a financial benefit that has a value of \$5,000 or more per year and is clearly unrelated to the project under review;
- ❖ Submitted by an applicant or small business with whom the member has longstanding scientific or personal differences that may be viewed as biasing the member's judgment;
- ❖ Submitted by a major competitor of the member; or
- ❖ If the member feels unable to provide objective advice.

The SRA is responsible for determining whether the participation of particular reviewers is appropriate, and for answering all questions about conflicts of interest.

IV. Confidentiality

All materials pertinent to the applications being reviewed are privileged communications prepared for use only by NIH consultants and NIH staff, and should not be shown to or discussed with other individuals. Reviewers' telephone inquiries, all correspondence, and requests for additional information regarding reviewed applications should be directed to the SRA. Reviewers are required to leave all review material with the SRA at the conclusion of the review meeting (except materials that are already in the public domain, e.g., reprints).

In accordance with NIH policy, all applications for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation

¹³ A close relative is defined as a parent, spouse/domestic partner, son or daughter.

¹⁴ A professional associate is defined as any colleague, scientific mentor, or student with whom the reviewer is currently conducting research or other professional activities or with whom the reviewer has personally worked within three years of the date of the review. The determination of a close professional association is a matter of judgment on the part of the SRA.

to view the internet sites.¹⁵ Reviewers are cautioned that their anonymity may be compromised when they directly access an Internet site.

V. Communication

The member composition of each Scientific Review Group (SRG) is posted on the NIH web site prior to the SRG meeting and is public information. However, applicants should not contact reviewers in any SRG about their application, the review process, nor should they send any related information to reviewers. If contacted by an applicant, reviewers are to refer all questions to the SRA or to IC program staff and must report any such contact to the SRA.

VI. Scientific Misconduct

Scientific misconduct is defined by the NIH as fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research. It does not include honest errors, honest differences in interpretations, or judgments of data. It also does not include unintentional failure to comply with federal requirements affecting specific aspects of the conduct of research, e.g., the protection of human subjects and the welfare of laboratory animals. It is vital that reviewers do not make allegations of potential scientific misconduct at the study section meeting or in their written critiques. Such concerns must be brought to the attention of the SRA in a confidential manner, preferably before the study section meets.

VII. Writing Your Review

"Formulae" do not exist for calculating an individual reviewer's score for an application. Rather, reviewers should balance the strengths and weaknesses of each application, using the criteria below.

A. All SBIR/STTR Applications (R41, R42, R43, and R44 designations)

Significance

- ❖ Does the proposed project have commercial potential to lead to a marketable product or process? Does this study address an important problem?
- ❖ What may be the anticipated commercial and societal benefits of the proposed activity?
- ❖ If the aims of the application are achieved, how will scientific knowledge be advanced?
- ❖ Does the application lead to enabling technologies (e.g., instrumentation, software) for further discoveries?
- ❖ Will the technology have a competitive advantage over existing/alternate technologies that can meet the market needs?

Approach

- ❖ Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project?
- ❖ Is the proposed plan a sound approach for establishing technical and commercial feasibility?
- ❖ Does the applicant acknowledge potential problem areas and consider alternative strategies?
- ❖ Are the milestones and evaluation procedures appropriate?

¹⁵ The NIH Guide Notice OD-00-004, namely "URL's in Applications, Proposals, or Appendices," at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-004.html>, presents the NIH policy on URL usage.

Innovation¹⁶

- ❖ Does the project challenge existing paradigms or employ novel technologies, approaches or methodologies?
- ❖ Are the aims original and innovative?

Investigators

- ❖ Is the Principal Investigator capable of coordinating and managing the proposed project?
- ❖ Is the work proposed appropriate to the experience level of the Principal Investigator and other researchers, including consultants and sub-awardees (if any)?
- ❖ Are the relationships of the key personnel to the small business and to other institutions appropriate for the work proposed?

Environment

- ❖ Is there sufficient access to resources (e.g., equipment, facilities, capabilities)?
- ❖ Does the scientific and technological environment in which the work will be done contribute to the probability of success?
- ❖ Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements?

B. Additional Criteria for Phase II Applications (Type 2R42 and Type 2R44 applications)

- ❖ How well did the applicant demonstrate progress toward meeting the Phase I objectives, demonstrating feasibility, and providing a solid foundation for the proposed Phase II activity?
- ❖ Did the applicant submit a concise Product Development Plan that adequately addresses the four areas described in Section I.C?
- ❖ Does the project carry a high degree of commercial potential, as described in the Product Development Plan?

C. Additional Criteria for Fast Track Applications (Type 1R42 and Type 1R44 applications)

- ❖ Does the Phase I application specify clear, appropriate measurable goals (milestones) that should be achieved prior to initiating Phase II?
- ❖ Did the applicant submit a concise Product Development Plan that adequately addresses the four areas described in Section I.C?
- ❖ To what extent was the applicant able to obtain letters of interest, additional funding commitments, and/or resources from the private sector or non-SBIR/STTR funding sources that would enhance the likelihood for commercialization?
- ❖ Does the project carry a high degree of commercial potential, as described in the Product Development Plan?

D. Additional Criteria for Amended Applications (applications with -A1 or -A2 suffixes)

- ❖ Are the responses to comments from the previous SRG review adequate?
- ❖ Do the changes improve the revised application?

¹⁶ Innovation is defined in PHS 2002-2 and PHS 398 as "Something new or improved, having marketable potential, including research for (1) development of new technologies, (2) refinement of existing technologies, or (3) development of new applications for existing technologies. For the purposes of PHS programs, an example of 'innovation' would be new medical or biological products, for improved value, efficiency, or costs."

E. Additional Criteria for Applications Involving Human Subjects Research

In accordance with NIH policy, the following five headings should be addressed in critiques of applications that propose the use of human subjects,¹⁷ and consideration of these points should be reflected in the priority score.

Protection of Human Subjects¹⁸ — *for all studies involving human subjects*

- ❖ If the application indicates that the proposed human subjects research is exempt from coverage by the regulations, determine if adequate justification is provided. If the claimed exemption is not justified, indicate "Unacceptable" and explain why you reached that conclusion.¹⁷
- ❖ What are the risks to human subjects recruited by the proposed study? Are the plans proposed for the protection of human subjects from research risks adequate, appropriate, and acceptable?
- ❖ Are the risks reasonable in relation to the anticipated benefits to the subjects and others? Are the risks reasonable in relation to the importance of the knowledge that reasonably may be expected to be gained?
- ❖ If all criteria are adequately addressed and there are no concerns, write "Acceptable risks and/or adequate protections." A brief explanation is advisable.
- ❖ If one or more criteria are inadequately addressed, write "Unacceptable risks and/or inadequate protections" and document the actual or potential issues that create the human subject concerns.

Data and Safety Monitoring Plan¹⁸ — *for clinical trials only*

- ❖ Does the applicant describe a Data and Safety Monitoring Plan that defines the general structure of the monitoring entity and mechanisms for the reporting of Adverse Events to the NIH and the IRB?

Inclusion of Women Plan¹⁸ Public law requires that women must be included in all NIH-sponsored clinical research projects unless a clear and compelling rationale establishes that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research.¹⁹

- ❖ Does the applicant include subject selection criteria and rationale?
- ❖ Does the applicant include a rationale for any exclusions?
- ❖ Does the applicant detail the enrollment dates?
- ❖ Does the applicant detail outreach strategies for recruitment?
- ❖ Does the proposed plan use the new tables to present the proposed composition?

Inclusion of Minorities Plan¹⁸ Public law requires that minorities must be included in all NIH-sponsored clinical research projects unless a clear and compelling rationale establishes that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research.¹⁹

- ❖ Does the applicant include subject selection criteria and rationale?
- ❖ Does the applicant include a rationale for any exclusions?
- ❖ Does the applicant detail the enrollment dates?

¹⁷ Reviewers should refer to the document "NIH Instructions to Reviewers for Evaluating Research Involving Human Subjects in Grant and Cooperative Agreement Applications" at http://grants.nih.gov/grants/peer/hs_review_inst.pdf.

¹⁸ Instructions to applicants concerning Human Subjects, the four required criteria, and the inclusion of women, minorities, and children are presented on pages 18-28, PHS 398 (<ftp://grants.nih.gov/forms/phs398.pdf>). Applicant organizations are NOT required to submit an Assurance or IRB approval at the time an application is submitted. An assurance number issued to a collaborator or contractor is not sufficient.

¹⁹ The 1997 Report of the NIH Director's Panel on Clinical Research (<http://www.nih.gov/news/crp/97report/execsum.htm>) adopted the following definition of Clinical Research: "(a) Patient-oriented research. Research conducted with human subjects (or on material of human origin such as tissues, specimens or cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects. This area of research includes: mechanisms of human disease, therapeutic interventions, clinical trials, and development of new technologies, (b) Epidemiological and behavioral studies, and (c) Outcomes research and health services research. Excluded from this definition are *in vitro* studies that utilize human tissues but do not deal directly with patients."

- ❖ Does the applicant detail outreach strategies for recruitment?
- ❖ Does the proposed plan use the new tables to present the proposed composition?

Inclusion of Children Plan¹⁸ NIH requires that children (individuals under the age of 21 years) of all ages be involved in all NIH-sponsored human subjects research unless there are scientific or ethical reasons for excluding them.

- ❖ Does the applicant describe the rationale for selecting/excluding specific age ranges?
- ❖ What is the expertise of the investigative team?
- ❖ Are the facilities for recruiting children appropriate?
- ❖ Are sufficient numbers of children included?

F. Human Subjects Codes

Each project involving human subjects must be assigned a code using the categories "1" to "4" below. Examine whether the gender, minority and children characteristics of the sample are scientifically acceptable, consistent with the aims of the project and comply with NIH policy. For each category, determine if the proposed subject recruitment targets are "A" (Acceptable) or "U" (Unacceptable). If you rate the sample as "U" consider this feature a weakness in the research design and reflect it in your overall score. Explain the reasons for the recommended codes; this is particularly critical for any item coded "U."²⁰ Category 5 for minority representation in the project means that only foreign subjects are in the study population, no United States subjects. If the study uses both, then use codes "1" through "4."

Category	Gender (G)	Minority (M)	Children (C)
1	Both Genders	Minority & non-minority	Children & adults
2	Only Women	Only minority	Only children
3	Only Men	Only non-minority	No children included
4	Gender Unknown	Minority representation unknown	Representation of children unknown
5		Only foreign subjects	

G. Additional Criteria

Biohazards — *may impact the priority score*

- ❖ Is the use of materials or procedures that are potentially hazardous to research personnel and/or the environment proposed?
- ❖ Is the proposed protection adequate?

Animal Welfare²¹ — *may impact the priority score*

- ❖ If vertebrate animals are involved, are adequate plans proposed for their care and use?
- ❖ Are the applicant's responses to the five required points²¹ appropriate?

²⁰ For example, proposed studies that involve men and women (over the age of 21), with only minority representation, would be designated "G1, M2, C3". If the reviewers found the representation of these groups to be scientifically acceptable, the studies would be designated "G1A, M2A, C3A". However, if the reviewers found the absence of non-minority subjects to be unacceptable in terms of the study design, the studies would be designated "G1A, M2U, C3A".

²¹ Instructions to applicants concerning Animal Welfare, including the five required points, are presented on page 28-29 of PHS 398 at <http://grants.nih.gov/grants/funding/phs398/phs398.pdf>. Applicant organizations that do not have an animal welfare Assurance on file with OLAW are NOT required to submit an Assurance Number or IACUC approval date at the time an application is submitted. An assurance number issued to a collaborator or contractor is neither acceptable nor sufficient.

- ❖ Will the procedures be limited to those that are unavoidable in the conduct of scientifically sound research?

Budget — *should NOT impact the priority score*

- ❖ For all applications, is the percent effort listed for the PI appropriate for the work proposed?
- ❖ On applications requesting up to \$100,000 total costs,³ is the overall budget realistic and justified in terms of the aims and methods proposed?
- ❖ On applications requesting over \$100,000 in total costs,³ is each budget category realistic and justified in terms of the aims and methods? Reviewers should provide justification for any modification in time or amount that they recommend.

H. Guide for Preparing Critiques

Follow the outline below and use the review criteria (Sections VII.A.-G.) to provide a comprehensive evaluation of each application's strengths and weakness. The goals of NIH-sponsored research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In your written review, you should comment on the following aspects of the application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. Written comments are included virtually verbatim in the Summary Statements that are sent to the applicants and to NIH program staff. The use of personal identifiers or offensive comments must be avoided.

Reviewers Critique

Significance: all applications

Approach: all applications

Innovation: all applications

Investigators: all applications

Environment: all applications

Progress in Phase I: Phase II applications only

Response to Previous Review: amended applications only

Product Development Plan: Phase II and Fast Track applications only

Protection of Human Subjects: all applications involving human subjects, to include

1) Risks to the Subjects;

2) Adequacy of Protection Against Risks;

3) Potential Benefits of the Proposed Research to the Subjects and Others;

4) Importance of the Knowledge to be Gained.

Data and Safety Monitoring Plan: clinical trials only

Inclusion of Women Plan: all applications involving clinical research

Inclusion of Minorities Plan: all applications involving clinical research

Inclusion of Children Plan: all applications involving human subjects

Human Subjects Codes: all applications involving human subjects

Animal Welfare: all applications involving vertebrate animals

Biohazards: only if a comment is warranted

Overall Evaluation: for each application, provide an overall evaluation of its strengths and weaknesses and a preliminary recommendation of its overall scientific and/or technical merit

Budget: all applications